EXHIBIT F

McGRAW-HILL DICTIONARY OF SCIENTIFIC AND TECHNICAL TERMS

Sixth Edition

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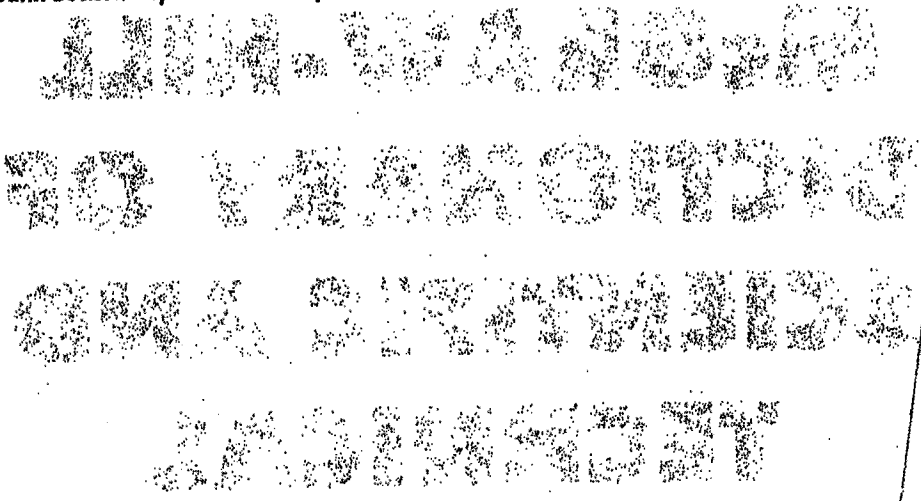
On the cover: Representation of a fullerene molecule with a noble gas atom trapped inside. At the Permian-Triassic sedimentary boundary the noble gases helium and argon have been found trapped inside fullerenes. They exhibit isotope ratios quite similar to those found in meteorites, suggesting that a fireball meteorite or asteroid exploded when it hit the Earth, causing major changes in the environment. *(Image copyright © Dr. Luann Becker. Reproduced with permission.)*



Over the six editions of the Dictionary, material has been drawn from the following references: G. M. Garrity et al., *Taxonomic Outline of the Procaryotes*, Release 2, Springer-Verlag, January 2002; D. W. Linzey, *Vertebrate Biology*, McGraw-Hill, 2001; J. A. Pechenik, *Biology of the Invertebrates*, 4th ed., McGraw-Hill, 2000; *U.S. Air Force Glossary of Standardized Terms*, AF Manual 11-1, vol. 1, 1972; F. Casey, ed., *Compilation of Terms in Information Sciences Technology*, Federal Council for Science and Technology, 1970; *Communications-Electronics Terminology*, AF Manual 11-1, vol. 3, 1970; P. W. Thrush, comp. and ed., *A Dictionary of Mining, Mineral, and Related Terms*, Bureau of Mines, 1968; *A DOD Glossary of Mapping, Charting and Geodetic Terms*, Department of Defense, 1967; J. M. Gilliland, *Solar-Terrestrial Physics: A Glossary of Terms and Abbreviations*, Royal Aircraft Establishment Technical Report 67158, 1967; W. H. Allen, ed., *Dictionary of Technical Terms for Aerospace Use*, National Aeronautics and Space Administration, 1965; *Glossary of Stinfo Terminology*, Office of Aerospace Research, U.S. Air Force, 1963; *Naval Dictionary of Electronic, Technical, and Imperative Terms*, Bureau of Naval Personnel, 1962; R. E. Huschke, *Glossary of Meteorology*, American Meteorological Society, 1959; *ADP Glossary*, Department of the Navy, NAVSO P-3097; *Glossary of Air Traffic Control Terms*, Federal Aviation Agency; *A Glossary of Range Terminology, White Sands Missile Range, New Mexico*, National Bureau of Standards, AD 467-424; *Nuclear Terms: A Glossary*, 2d ed., Atomic Energy Commission.

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than that of the speed of sound in the fluid. Also known as subcritical flow. { ¦səb'sän·ik 'flō }

subsonic inlet [ENG] An entrance or orifice for the admission of fluid flowing at speeds less than the speed of sound in the fluid. { ¦səb'sän·ik 'in,let }

subsonic nozzle [ENG] A nozzle through which a fluid flows at speed less than the speed of sound in the fluid. { ¦səb'sän·ik 'näz·əl }

subsonic speed [FL MECH] A speed relative to surrounding fluid less than that of the speed of sound in the same fluid. { ¦səb'sän·ik 'spēd }

subspace [MATH] A subset of a space which, in the appropriate context, is a space in its own right. { 'səb,spās }

subspecies [SYST] A geographically defined grouping of local populations which differs taxonomically from similar subdivisions of species. { ¦səb'spē·shēz }

substance [PHYS] Tangible material, occurring in macroscopic amounts. { 'səb·stəns }

substance P [BIOCHEM] An undecapeptide widely distributed in the central nervous system and found in highest concentrations in superficial layers of the dorsal horn of the spinal cord, in the trigeminal nerve nucleus, and in the substantia nigra; acts as a neurotransmitter. { 'səb·stəns 'pē }

substandard propagation [ELECTROMAG] The propagation of radio energy under conditions of substandard refraction in the atmosphere; that is, refraction by an atmosphere or section of the atmosphere in which the index of refraction decreases with height at a rate of less than 12 N units (unit of index of refraction) per 1000 feet (304.8 meters). { ¦səb'stan·dərd ,präp·ə'gā·shən }

substantive dye *See* direct dye. { 'səb·stən·tiv 'dī }

substation [ELEC] *See* electric power substation. [ENG] An intermediate compression station to repressure a fluid being transported by pipeline over a long distance. [MIN ENG] A subsidiary station for the conversion of power to the type, usually direct current, and voltage needed for mining equipment and fed into the mine power system. { 'səb,stā·shən }

substellar object *See* brown dwarf. { ,səb,stel·ər 'äb,jekt }

substellar point [ASTRON] The geographical position of a star; that point on the earth at which the star is in the zenith at a specified time. Also known as subastral point. { ¦səb'stel·ər 'pȯint }

substituent [ORG CHEM] An atom or functional group substituted for another in a chemical structure. { səb'stich·ə·wənt }

substitute mode [COMPUT SCI] One method of exchange buffering, in which segments of storage function alternately as buffer and as program work area. { 'səb·stə,tüt ,mōd }

substitution [PSYCH] A defense mechanism whereby an unattainable or unacceptable goal, emotion, or object is replaced by one that is more attainable or acceptable. { ,səb·stə'tü·shən }

substitutional impurity [SOLID STATE] An atom or ion which is not normally found in a solid, but which resides at the position where an atom or ion would ordinarily be located in the lattice structure, and replaces it. { ,səb·stə'tü·shən·əl im'pyu̇r·əd·ē }

substitution alphabet [COMMUN] An alphabet used in a coded message in which each letter in the original message is replaced by another letter in the coded message, according to a set of rules. { ,səb·stə¦tü·shən 'al·fə,bet }

substitution cipher [COMMUN] A cipher in which the characters of the original message are replaced by other characters according to a key. { ,səb·stə'tü·shən ,sī·fər }

substitution group *See* permutation group. { ,səb·stə'tü·shən ,grüp }

substitution method [PHYS] Any method of measurement, such as substitution weighing, in which a quantity is determined by substituting for it a known quantity which produces the same effect. { ,səb·stə'tü·shən ,meth·əd }

substitution reaction [CHEM] Replacement of an atom or radical by another one in a chemical compound. { ,səb·stə'tü·shən rē,ak·shən }

substitution solid solution [MET] A solid alloy having the atoms of the solute located at some lattice of points of the solvent. { ,səb·stə'tü·shən 'säl·əd sə'lü·shən }

substitution weighing [MECH] A method of weighing to allow for differences in lengths of the balance arms, in which the object to be weighed is first balanced against a counterpoise, and the known weights needed to balance the same counterpoise are then determined. Also known as counterpoise method. { ,səb·stə'tü·shən ,wā·iŋ }

substitutive nomenclature [ORG CHEM] A system in which the name of a compound is derived by using the functional group (the substituent) as a prefix or suffix to the name of the parent compound to which it is attached; for example, in 2-chloropropane a chlorine atom has replaced a hydrogen atom on the central carbon of the propane chain. { ,səb·stə,tüd·iv 'nō·mən,klā·chər }

substrain [CELL MOL] A strain derived by isolation of a single cell or group of cells having properties or markers not shared by the other cells of the cell strain. { 'səb·,strān }

substrate [BIOCHEM] The substance with which an enzyme reacts. [ECOL] The foundation to which a sessile organism is attached. [ELECTR] The physical material on which a microcircuit is fabricated; used primarily for mechanical support and insulating purposes, as with ceramic, plastic, and glass substrates; however, semiconductor and ferrite substrates may also provide useful electrical functions. [ENG] Basic surface on which a material adheres, for example, paint or laminate. [ORG CHEM] A compound with which a reagent reacts. { 'səb,strāt }

substratosphere [METEOROL] A region of indefinite lower limit just below the stratosphere. { ¦səb'strad·ə,sfir }

substratum [GEOL] Any layer underlying the true soil. { ¦səb'strad·əm }

substring [COMPUT SCI] A sequence of successive characters within a string. { 'səb,striŋ }

substructure [CIV ENG] The part of a structure which is below ground. { ¦səb'strək·chər }

subsurface contour *See* structure contour. { ¦səb'sər·fəs 'kän,tu̇r }

subsurface current [OCEANOGR] An ocean-water current which is not present at the surface or whose core (region of maximum velocity) is below the surface. { ¦səb'sər·fəs 'kə·rənt }

subsurface flow [HYD] Interflow plus groundwater flow. { ¦səb'sər·fəs 'flō }

subsurface geology [GEOL] The study of geologic features beneath the land or sea-floor surface. Also known as underground geology. { ¦səb'sər·fəs jē'äl·ə·jē }

subsurface irrigation [AGR] A method of providing water to plants by raising the water table to the root zone of the crop or by carrying moisture to the root zone by perforated underground pipe. Also known as subirrigation. { ,səb,sər·fəs ,ir·ə'gā·shən }

subsurface radar *See* ground-probing radar. { ,səb,sər·fəs 'rā·där }

subsurface tillage [AGR] A method of stirring the soil with blades that leaves stubble on or just below the surface. { ¦səb'sər·fəs 'til·ij }

subsurface waste disposal [ENG] A waste disposal method for manufacturing wastes in porous underground rock formations. { ¦səb'sər·fəs 'wāst di,spōz·əl }

subsurface wave [ELECTROMAG] Electromagnetic wave propagated through water or land; operating frequencies for communications may be limited to approximately 35 kilohertz due to attenuation of high frequencies. { ¦səb'sər·fəs 'wāv }

subsynchronous [ELEC] Operating at a frequency or speed that is related to a submultiple of the source frequency. { ¦səb'siŋ·krə·nəs }

subsynchronous resonance [ELEC] An electrical resonant frequency on an alternating-current transmission line that is less than the line frequency, and results from the insertion of series capacitors to cancel out part of the line and system reactance. { səb¦siŋ·krə·nəs 'rez·ən·əns }

subsystem [ENG] A major part of a system which itself has the characteristics of a system, usually consisting of several components. { 'səb,sis·təm }

subtangent [MATH] For a given point on a plane curve, the projection on the *x* axis of a rectangular coordinate system of the segment of the tangent between the point of tangency and the intersection of the tangent with the *x* axis. { ¦səb'tan·jənt }

subtend [BOT] To lie adjacent to and below another structure, often enclosing it. [MATH] A line segment or an arc of a circle subtends an angle with vertex at a specified point if the end points of the line segment or arc lie on the sides of the angle. { səb'tend }

from a new target in radar and sonar. **2.** *See* acquire. { 'tär·gət ˌak·wə'zish·ən }

target acquisition radar [ENG] An antiaircraft artillery radar, normally of lesser range capabilities but of greater inherent accuracy than that of surveillance radar, whose normal function is to acquire aerial targets either by independent search or on direction of the surveillance radar, and to transfer these targets to tracking radars. { 'tär·gət ˌak·wə'zish·ən ˌrā,där }

target analysis [ORD] Examination of potential targets to determine their military importance, their relative priority for attack, and the capabilities of available weapons for such attack. { 'tär·gət ə,nal·ə·səs }

target angle [NAV] The relative bearing of one craft from another craft, measured clockwise through 360°. [ORD] The angle at the target subtended by the observing base line. { 'tär·gət ˌaŋ·gəl }

target approach point [AERO ENG] In air transport operations, a navigational checkpoint over which the final turn-in to the drop zone-landing zone is made. { 'tär·gət ə'prōch ˌpȯint }

target array [ORD] A graphic representation of enemy forces, personnel, and facilities in a specific situation, accompanied by a target analysis. { 'tär·gət ə,rā }

target bearing [ORD] **1.** The true compass bearing of a target from a firing ship. **2.** The bearing of a target measured in the horizontal from the bow of one's own ship clockwise from 0 to 360°, or from the nose of one's own aircraft in hours of the clock. { 'tär·gət ˌber·iŋ }

target cell [PHYSIO] A cell that has receptors for the product of a signaling cell. { 'tär·gət ˌsel }

target central processing unit [COMPUT SCI] The type of central processing unit for which a language processor (assembler, compiler, or interpreter) generates machine language output. { 'tär·gət ˌsen·trəl ˌpräs·es·iŋ ˌyü·nət }

target compound [ORG CHEM] In chemical synthesis, the molecule of interest. { 'tär·gət ˌkäm,paůnd }

target concentration [ORD] A grouping of geographically proximate targets. { 'tär·gət ˌkän·sən,trā·shən }

target configuration [COMPUT SCI] The combination of input, output, and storage units and the amount of computer memory required to carry out an object program. { 'tär·gət kən,fig·yə,rā·shən }

target cross section *See* echo area. { 'tär·gət 'krȯs ˌsek·shən }

target-designating system [ELECTR] A system for designating to one instrument a target which has already been located by a second instrument; it employs electrical data transmitters and receivers which indicate on one instrument the pointing of another. { 'tär·gət ˌdez·ig,nād·iŋ ˌsis·təm }

target deviation [ORD] Distance from point of impact or point of burst to the target. { 'tär·gət ˌdē·vē'a·shən }

target discrimination [ELECTR] The ability of a detection or guidance system to distinguish a target from its background or to discriminate between two or more targets that are close together. { 'tär·gət di,skrim·ə,nā·shən }

target drone [AERO ENG] A pilotless aircraft controlled by radio from the ground or from a mother ship and used exclusively as a target for antiaircraft weapons. { 'tär·gət ˌdrōn }

target echo [ELECTROMAG] A radio signal reflected by an airborne or other target and received by the radar station which transmitted the original signal. { 'tär·gət ˌek·ō }

target glint *See* scintillation. { 'tär·gət ˌglint }

target identification [ORD] The act of determining the nature of a target, including whether it is a friend or foe. { 'tär·gət ī,den·tə·fə'kā·shən }

target indicating system [ORD] A system which indicates to the tracker of an antiaircraft automatic weapon the direction of approach of a suitable target, or the approach of a new target after engagement with one target has been broken off. { 'tär·gət 'in·də,kād·iŋ ˌsis·təm }

target information center [ORD] An intelligence center set up afloat or ashore for assembly, evaluation, interpretation, dissemination, and coordination of target information for supporting weapons, that is, artillery, naval gunfire, and air strike. { 'tär·gət ˌin·fər,mā·shən ˌsen·tər }

target language [COMPUT SCI] The language into which a program (or text) is to be converted. { 'tär·gət ˌlaŋ·gwij }

target length [ORD] Length of a target as it appears to an observer or gunner at the moment the gun is fired. { 'tär·gət ˌleŋkth }

target noise [ELECTROMAG] Statistical variations in a radar echo signal due to the presence on the target of a number of reflecting elements randomly oriented in space; target noise can cause scintillation. { 'tär·gət ˌnȯiz }

target offset [ORD] Horizontal angle at the target between a line from the target to the piece and a line from the target to the observation post. { 'tär·gət ˌȯf,set }

target of opportunity [ORD] **1.** A target visible to a surface or air sensor or observer, which is within range of available weapons and against which fire has not been scheduled or requested. **2.** A nuclear target observed or detected after an operation begins that has not been previously considered, analyzed, or planned for a nuclear strike. { 'tär·gət əv ˌäp·ər'tü·nəd·ē }

target pack [COMPUT SCI] A disk pack that is used to maintain systems software and, in particular, to hold a copy of a system control program on which modifications are made and tested. { 'tär·gət ˌpak }

target pattern [AERO ENG] The flight path of aircraft during the attack phase. { 'tär·gət ˌpad·ərn }

target phase [COMPUT SCI] The stage of handling a computer program at which the object program is first carried out after it has been compiled. { 'tär·gət ˌfāz }

target program *See* object program. { 'tär·gət ˌprō,gram }

target range [ORD] Area equipped for practice in shooting at targets. { 'tär·gət ˌrānj }

target response [ORD] The effect on men, material, and equipment of blast, heat, light, and nuclear radiation resulting from the explosion of a nuclear weapon. { 'tär·gət ri,späns }

target routine *See* object program. { 'tär·gət rü,tēn }

target scintillation *See* scintillation. { 'tär·gət ˌsint·əl'ā·shən }

target seeker [ORD] **1.** A missile having a self-contained system that provides homing guidance to the target. Also known as homer. **2.** The device within such a missile that directs it to the target. { 'tär·gət ˌsēk·ər }

target selector [ORD] Component of both a target-designating system and a target-indicating system; it is an off-carriage observing instrument provided for the purpose of selecting an initial or new target, and it is electrically connected to the gun mount in such a manner as to slew the gun to the approximate azimuth and elevation of a selected target (when the selector is a component of a target-designating system), and to give the tracker an indication of the direction of approach of selected target (when the selector is a component of a target-indicating system). { 'tär·gət si,lek·tər }

target signal [ELECTROMAG] The radio energy returned to a radar by a target. Also known as echo signal; video signal. { 'tär·gət ˌsig·nəl }

target signature [ELECTR] Characteristic pattern of the target displayed by detection and classification equipment. { 'tär·gət ˌsig·nə·chər }

target spot [PL PATH] Any plant disease characterized by lesions in the form of concentric markings. { 'tär·gət ˌspät }

target spotter [ORD] Small, black metal disk attached to a target in practice shooting to show the shooter exactly where the bullet has hit. { 'tär·gət ˌspäd·ər }

target strength [ACOUS] A measure of the reflecting power of a sonar target, which is expressed in decibels by the equation $E + 2L - S$, where E is the echo level, L is the total transmission loss, and S is the source level. { 'tär·gət ˌstrenkth }

target system [ORD] **1.** All the targets situated in a particular geographic area and functionally related. **2.** A group of targets which are so related that their destruction will produce some particular effect desired by the attacker. { 'tär·gət ˌsis·təm }

target timing [NAV] The timing of successive positions of a radar target, as plotted on a polar coordinate diagram, for the purpose of determining ground speed and track of a craft. { 'tär·gət ˌtīm·iŋ }

target-type flowmeter [ENG] A fluid-flow measurement device with a small circular target suspended centrally in the flow conduit; the target transmits force to a force-balance transmitter by means of a pivoted bar. { 'tär·gət ˌtīp 'flō,mēd·ər }

target volume [ELECTROMAG] The volume of that part of a precipitation-type radar target from which a target signal is received; if the precipitation completely fills the radar beam,

EXHIBIT G

#14C/RW

PATENT
File No. 1000.1b10

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: FODOR, et al.	Art Unit: 1656
Application No.: 10/098,203	Examiner: J. Riley
Filed: 3/15/2002	
For: NUCLEIC ACID READING AND ANALYSIS SYSTEM	RESPONSE AND RECORD OF TELEPHONIC INTERVIEW

Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action dated December 23, 2002 (Paper no. 13) please reconsider the rejections in light of the following amendments and remarks.

IN THE CLAIMS

105. (Amended) A polynucleotide analysis apparatus comprising:

a capillary substrate having a surface that is made of a material that is different from the substrate, said surface comprising a plurality of different polynucleotides, each of said different polynucleotides occupying a different area of said surface, each of said areas being 10^{-1} cm^2 or less in detectable area, said surface comprising more than 10 of such polynucleotides, at least some of said polynucleotides bearing fluorescently labeled target molecules excitable with a laser;

C1
548
D1

SUB D1 CONT. D

an argon laser light source capable of generating light at a wavelength of about 488 nm or less at said surface to excite said fluorescently labeled target molecules, which generate light at a frequency greater than 488 nm;

said laser oriented to direct the laser light at said surface at an angle capable of contacting said target molecules;

a CCD detector oriented in a manner capable of detecting light fluoresced from said target molecules in said areas;

and

a data collection, recording and management system for storing fluoresced light intensity, said data collection, recording and management system coupled to said CCD detector, said data collection, recording and management system storing light intensity and converting said light intensity into nucleic acid sequence information.

C2 SUB E1

~~107~~ 108. (Amended) A polynucleotide analysis apparatus in accordance with claim ~~105~~ 1 wherein the surface is a gel.

C3

~~106~~ 111. (Amended) A polynucleotide analysis apparatus comprising an argon laser light source capable of generating a laser beam providing light at a wavelength of about 488 nm or less to excite fluorescently labeled target molecules attached to said polynucleotides in a substrate to emit excited fluorescent light at a wavelength greater than 488 nm detected by a CCD detector oriented in a manner capable of detecting said emitted fluorescent light from said target molecules in said substrate irradiated by said laser beam, said substrate having more than 10 polynucleotides and each detectable polynucleotide being present in 10^{-1}cm^2 or less in detectable area, said CCD detector coupled to a data collection system for analyzing fluoresced light intensity and converting said light intensity into nucleic acid sequence information.

SUB E1

~~108~~ 112. (Amended) A polynucleotide analysis apparatus in accordance with claim ~~107~~ 111 wherein the substrate is a plurality of capillaries.

Sub E1 C3 cont. 9 ~~113.~~ 8 (Amended) A polynucleotide analysis apparatus in accordance with claim ~~112~~ 8 wherein the substrate further comprises a gel or polymer.

Sub E1 C4 13 ~~118.~~ 8 (Amended) A polynucleotide analysis apparatus in accordance with claim ~~112~~ 8 wherein said fluorescently labeled target molecules are within the capillaries.

46 ~~151.~~ 55 (Amended) A method in accordance with claim ~~140~~ 55 comprising providing 100,000 beads.

C5 Sub E1 ~~141~~ 152. 143 (Amended) A method in accordance with claim ~~148~~ 143 comprising providing 100,000 beads.

REMARKS

The present application contains claims 105 to 156. The Examiner has rejected claims 106, 113, 151, and 152 under 35 U.S.C. 112, second paragraph. Claims 105-110 and 112-156 are rejected under 35 U.S.C. 112, first paragraph. Claim 111 is allowed. Applicants have amended claims 113, 151, 152 to clarify the language of those claims and offer further remarks below for the remaining rejections.

Applicants wish to express their thanks to the Examiner for conducting an interview on January 15, 2003. In that interview, Applicant's attorney discussed the claim amendments made in this response and reviewed the 112, first paragraph rejections. No agreements regarding the claims were made and Applicant's attorney advised the Examiner that the substance of the conversation was to be embodied in the present response. The Examiner requested extra copies of the four previously filed 1449 forms (dated 12/4/02, 10/16/02, 8/20/02 and 5/30/02) and those are attached.

DISCUSSION

Rejections under 35 USC 112, second paragraph

Applicants have amended claims 108, 112 and 113 to parallel the language in claims 105, 108 and 111. Claims 151 and 152 have been amended to correct the dependency and are in a method format. Additionally, Applicants have made some minor clarifications in claims 105, 111 and 118.

Regarding claim 106, the word "translated" in the phrase "translated relative to the laser light" is construed to mean "moved" relative to one another.

Rejections under 35 USC 112, first paragraph

The examiner has rejected claim 105, 112, 119, and 144 under 35 USC 112, second paragraph. The passage at page 20, line 25 to page 22, line 5 is relevant to many of these claims. Page 20, line 34 shows that "capillaries" can be a substrate (Claim 112). Regarding claim 105, page 21, lines 26 and 27 state that surfaces can be composed of material that is different from the substrate, and lines 29 to 33 state that the surface can comprise some specific materials "or any of the above-listed substrate materials" including "gels" at page 20, line 33. Consequently, the substrate can be a capillary and the surface of the substrate can be a gel. Page 20, line 34 states that "spheres" can be substrates, page 14, line 13 states that "beads" can be substrates. It is intended that these spheres or beads be the carriers of one type of nucleic acid for analysis and "1,000" (shown as "10^3") sequences on a support is shown on page 29, line 22.

Page 5, lines 14 to 25 shows that a "receptor" is contacted with a substrate (lines 17-18), the receptors can be nucleic acids (page 13, lines 7-9), the receptor is labeled with a fluorescent molecule (page 5, lines 20-21). As shown above, beads are substrates. See also page 6, lines 15-21, page 12, lines 24 to page 13, line 7, page 35, lines 13-17, and other locations. Therefore, it is clear that a fluorescent label can be attached to a nucleic acid which is then contacted with the substrate bead as in claim 144.

CONCLUSION

Applicants have addressed all outstanding rejections and believe that the present claims are in condition for allowance. Applicants hereby request reconsideration and withdrawal of the rejections. Applicants believe that no fees are due, however, the Commissioner is authorized to charge any fees or credit any overpayments associated with this application to Deposit Account No. 01-0431.

Dated: 1-17-03

Respectfully submitted,

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Appendix A
Mark-up of pending claims

105. (Amended) A polynucleotide analysis apparatus comprising:

a capillary [in contact with] substrate having a [substrate] surface that is made of a material that is different from the substrate, said [substrate] surface comprising a plurality of different polynucleotides, each of said different polynucleotides occupying a different area of said [substrate] surface, each of said areas being 10^{-1} cm^2 or less in detectable area, said [substrate] surface comprising more than 10 of such polynucleotides, at least some of said polynucleotides bearing fluorescently labeled target molecules excitable with a laser;

an argon laser light source capable of generating light at a wavelength of about 488 nm or less at said [substrate] surface to excite said fluorescently labeled target molecules, which generate light at a frequency greater than 488 nm;

said laser oriented to direct the laser light at said [substrate] surface at an angle capable of contacting said target molecules;

a CCD detector oriented in a manner capable of detecting light fluoresced from said target molecules in said areas;

and

a data collection, recording and management system for storing fluoresced light intensity, said data collection, recording and management system coupled to said CCD detector, said data collection, recording and management system storing light intensity and converting [translating] said light intensity into nucleic acid sequence information.

108. (Amended) A polynucleotide analysis apparatus in accordance with claim 105 wherein the [substrate] surface is a gel.

111. (Amended) A polynucleotide analysis apparatus comprising an argon laser light source capable of generating a laser beam providing light at a wavelength of about 488 nm or less to excite fluorescently labeled target molecules attached to said

polynucleotides in a substrate to emit excited fluorescent light at a wavelength greater than 488 nm detected by a CCD detector oriented in a manner capable of detecting said emitted fluorescent light from said target molecules in said substrate irradiated by said laser beam, said substrate having more than 10 polynucleotides and each detectable polynucleotide being present in $10^{-1}cm^2$ or less in detectable area, said CCD detector coupled to a data collection system for analyzing fluoresced light intensity and [translating] converting said light intensity into nucleic acid sequence information.

112. (Amended) A polynucleotide analysis apparatus in accordance with claim 111 wherein the substrate is [in contact with] a plurality of capillaries.

113. (Amended) A polynucleotide analysis apparatus in accordance with claim 112 wherein the substrate further comprises a gel or polymer.

118. (Amended) A polynucleotide analysis apparatus in accordance with claim 112 wherein said [substrate is] fluorescently labeled target molecules are within the capillaries.

151. (Amended) A method in accordance with claim [132] 140 [wherein there are] comprising providing 100,000 beads.

152. (Amended) A method in accordance with claim [149] 148 [wherein there are] comprising providing 100,000 beads.

EXHIBIT H

Attorney Docket No.: 56297-5003-19

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application: Stephen P.A. FODOR *et al.*	)	
Application No.: 10/125,530	)	Group Art Unit: 1634
Filed: April 19, 2002	)	
For Arrays for Detecting Nucleic Acids	)	Examiner: Goldberg, J.A.

Commissioner for Patents
U.S. Patent and Trademark Office
2011 South Clark Place
Customer Window, Mail Stop Amendment
Crystal Plaza Two, Lobby, Room 1B03
Arlington, VA 22202

REPLY TO OFFICE ACTION
PURSUANT TO 37 CFR §1.111

This Reply is responsive to the Office Action dated May 19, 2004, the time period for response to which expires August 19, 2004. Entry of the following remarks and reconsideration of the claimed subject matter is respectfully requested.

Please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 7 of this paper.

IN THE CLAIMS:

Please cancel claim 27 without prejudice or disclaimer.

Please add new claims 68-73.

26. (Currently Amended) An apparatus for analyzing nucleic acid binding, comprising:

a substrate having a surface that comprises at least 1000 ~~different~~ spheres, beads, or particles, wherein each of the at least 1000 spheres, beads or particles comprises a ~~having different~~ unique species of nucleic acids directly or indirectly attached thereto~~,wherein the area of the substrate where the at least 1000 spheres, beads, or particles are located is less than 1 cm² and wherein the substrate has a surface~~.

27-29. (Cancelled)

30. (Previously Presented) An apparatus in accordance with claim 26 wherein the area of the substrate is less than 10^{-1}cm².

31. (Previously Presented) An apparatus in accordance with claim 26 wherein the substrate comprises beads.

32. (Previously presented) An apparatus in accordance with claim 26 wherein the substrate comprises spheres.

33. (Previously presented) An apparatus in accordance with claim 26 wherein the substrate comprises particles.

34. (Currently Amended) An apparatus in accordance with claim 26 wherein the substrate comprises at least about 10,000 ~~different~~ spheres, beads, or particles.

35. (Currently Amended) An apparatus in accordance with claim 26 wherein the substrate comprises at least about 100,000 ~~different~~ spheres, beads or particles.

36-38. (Canceled)

39. (Previously Presented) An apparatus in accordance with claim 26 wherein the substrate or its surface is composed of a polymer, plastic, a resin, silica or silica-based materials, carbon, metals, or inorganic glasses.

40. (Previously Presented) An apparatus in accordance with claim 39 wherein the substrate or its surface is composed of a polymer.

41. (Previously Presented) An apparatus in accordance with claim 39 wherein the substrate or its surface is composed of silica.

42. (Currently Amended) A substrate that comprises at least 1000 ~~different~~ spheres, beads or particles on its surface, wherein each of the 1000 spheres, beads or particles comprises a ~~having different~~ unique species of nucleic acids ~~attached thereto, wherein the area of the substrate where the~~ on the ~~at least 1000 spheres, beads, or particles are located is less than 1 cm^2 and wherein the substrate has a surface~~.

43-44. (Canceled)

45. (Previously Presented) A substrate in accordance with claim 42 wherein the substrate comprises beads.

46. (Previously Presented) A substrate in accordance with claim 42 wherein the substrate comprises spheres.

47. (Previously Presented) A substrate in accordance with claim 42 wherein the substrate or its surface is composed of a polymer, plastic, a resin, silica or silica-based materials, carbon, metals, or inorganic glasses.

48. (Currently Amended) A substrate in accordance with claim 42 wherein the substrate comprises at least about 10,000 ~~different~~ spheres, beads, or particles.

49. (Currently Amended) A substrate in accordance with claim 42 wherein the substrate comprises at least about 100,000 ~~different~~ spheres, beads or particles.

50. (Previously Presented) A substrate in accordance with claim 42 wherein the area of the substrate is less than 10^{-1} cm^2.

51. (Previously Presented) A substrate in accordance with claim 42 wherein the area of the substrate is less than 10^{-2} cm^2.

52. (Currently Amended) A method for screening large numbers of biological polymers, comprising:

providing target nucleic acids;

providing a substrate having an array of at least 1000 ~~different~~ spheres, beads or particles~~, the different~~ wherein each of the at least 1000 spheres, beads or particles comprises a unique species of nucleic acid; ~~spheres, beads or particles occupying an area on a substrate of less than 1 cm^2, wherein the substrate has a surface, and at least some of the different spheres, beads or particles having different nucleic acids attached thereto;~~

contacting the target nucleic acids with the spheres, beads or particles under hybridization conditions so that, after contact, at least some of the nucleic acids on the spheres, beads or particles hybridize to the target nucleic acids and

determining which spheres, beads or particles have nucleic acids that are bound to target nucleic acids.

53-54. (Canceled)

55. (Previously Presented) A method in accordance with claim 52 wherein the substrate or its surface is composed of a polymer, plastic, a resin, silica or silica-based materials, carbon, metals, or inorganic glasses.

56. (Canceled)

57. (Currently Amended) A method in accordance with claim 52 wherein the nucleic acids attached to the spheres, beads or particles are oligonucleotides.

58. (Previously Presented) A method in accordance with claim 52 wherein the substrate comprises at least about 10,000 spheres, beads or particles.

59-60 (Canceled)

61. (Previously Presented) A method in accordance with claim 52 wherein the area of the substrate is less than 10^{-1} cm^2.

62. (Previously Presented) A method in accordance with claim 52 wherein the area of the substrate is less than 10^{-2} cm^2.

63. (Previously Presented) A substrate according to claim 42 wherein the substrate comprises particles.

64. (Previously Presented) An apparatus of claim 26 wherein the nucleic acids are oligonucleotides.

65. (Previously Presented) A substrate of claim 42 wherein the nucleic acids are oligonucleotides.

66. (Previously Presented) A substrate of claim 42 wherein the nucleic acids are indirectly attached to the spheres, beads or particles.

67. (Previously Presented) A method of claim 52 wherein the substrate comprises at least about 100,000 spheres, beads or particles.

68. (New) An apparatus in accordance with claim 26 wherein the spheres, beads or particles are coded.

69. (New) An apparatus in accordance with claim 26 wherein the spheres, beads or particles are coded to indicate their sequence specificity.

70. (New) An apparatus in accordance with claim 42 wherein the spheres, beads or particles are coded.

71. (New) An apparatus in accordance with claim 42 wherein the spheres, beads or particles are coded to indicate their sequence specificity.

72. (New) A method in accordance with claim 52 wherein the spheres, beads or particles are coded.

73. (New) A method in accordance with claim 52 wherein the spheres, beads or particles are coded to indicate their sequence specificity.

REMARKS

Claims 26, 30-35, 39-42, 45-52, 55, 57-58, 61-73 are pending. The Examiner has rejected the pending claims under 35 U.S.C. §112, first paragraph for various reasons discussed below. The same claims were also rejected under 35 U.S.C. §112, second paragraph mainly due to the recitation of the word "different." Claims 26, 31-33, 39, 41-42, and 45-47 are rejected under 35 U.S.C. §102(b), as anticipated by Matteucci *et al.* (*J. Am. Chem. Soc.* Vol. 1981, pages 3185-3191, 1981). Applicants address the rejections below.

Applicants have added six new claims (claims 68-73) which are supported at page 37, lines 6-20).

Examiner Interview

Applicants thank Examiner Goldberg, Examiner Forman and SPE Jones for the helpful interview held on April 7 with Mr. Phil McGarrigle and Applicant's representative Michael Tuscan.

In the interview, Applicants discussed the process and reasoning on the part of the U.S. PTO for withdrawing the application from issue after payment of the issue fee on October 17, 2003. Examiner Goldberg indicated that potential new matter issues in the allowed claims may need to be addressed by the Office. The Examiner had not completed her review of the application at the time of the interview and no agreement was reached concerning the Examiner's concerns or the pending claims.

New Matter Rejections

Claims 26-27, 30-35, 39-42, 45-51 have been rejected under 35 U.S.C. §112, first paragraph. Applicants address each of the noted rejections in the order presented in the Office Action.

1. Numbers of spheres, beads or particles in the claims and the differences between the at least 1,000 spheres, beads or particles.

The Examiner states that the "specification does not appear to contemplate 1000 different spheres, beads or particles" (page 2, line 20) and does not indicate "what the difference between the spheres would be..." (page 3, line 15). Applicants respectfully disagree and for clarity have amended each of independent claims 26, 42 and 52 to recite "at least 1,000 spheres, beads or particle, wherein each of the at least 1000 spheres, beads or particles comprises a unique species of nucleic acid." Accordingly, the claims require that each of the at least 1000 spheres, beads or particles differ from each other by the unique species (sequence) of attached nucleic acid. In other words, the at least 1,000 spheres beads or particles as claimed have at least 1,000 unique species of nucleic acid attached thereto, one species per bead.

Applicants also note that the Examiner has rejected the use of "different" to modify the terms "spheres, beads, or particles." She has also suggested that removing "different" would overcome this rejection. Without necessarily agreeing with the propriety of the rejection, Applicants thank the Examiner for her suggestion and follow her advice. Applicants respectfully assert that the scope of the claims is not lessened by the deletion of "different."

2. The support for beads, spheres or particles provided on a surface and quantity and density of the claimed beads, spheres or particles.

The Examiner states that the "specification does not appear to contemplate that regions may be beads or spheres or particles" . . . or density of beads," or "the specification does not appear to teach a quantity or density of beads" (page 2, line 20 to page 3, line 10). Applicants respectfully disagree. As the Examiner has noted, the specification discloses that beads may be used as the substrate or support for nucleic acids. The specification is generally organized to discuss various methods of synthesizing or attaching polymers, such as oligonucleotides, at high density to a substrate. The specification then discusses different substrates, including beads, that may

be used. Concerning the general organization of the specification, the first paragraph of the "General" description section of the specification (page 10, lines 3-5) states that:

> "The present invention relies in part on the ability to synthesize or attach specific recognition reagents at known locations on a substrate, typically a single substrate. In particular, the present invention provides the ability to prepare a substrate having a very high density matrix pattern of positionally defined specific recognition reagents." [Emphasis added.]

One method that can be used to attach nucleic acids to the substrate is the VLSIPS method as described in the present application and shown in U.S. Patent No. 5, 143,854, which is incorporated by reference on the first page of the instant application. For instance, page 12 (lines 22-36) of the present application discloses that VLSIPS can be used to create large numbers of different oligonucleotide probes on a substrate. Specifically, the specification states that "VLSIPS technology allows the production of a very large number of different oligonucleotide probes to be simultaneously and automatically synthesized including numbers in excess of about 10^4, 10^5, 10^6, 10^7, 10^8, or even more," (page 12, lines 32-36). Each oligonucleotide species is typically attached in a "region" of the substrate (see page 12, lines 9-12, "the VLSIPS technology allows the production of a substrate with a high density matrix of positionally mapped regions with specific recognition reagents attached at each distinct region." [Emphasis added.]) The specification also teaches that other methods, such as caged biotin, may be used to attach preformed nucleic acids to a substrate in the same amounts or density (see page 33, last paragraph).

Different substrates to which the oligonucleotides may be attached are discussed at page 14, starting at line 25 (material incorporated by reference from U.S. Patent 5,143,854, and added to the instant specification at this page and line in the Second Preliminary Amendment dated January 11, 2003). In this section, the specification discloses that:

> Essentially, any conceivable substrate may be employed in the invention. The substrate may be biological, nonbiological, organic, inorganic, or a combination of any of these, existing as particles, strands, precipitates, gels, sheets, tubing, spheres, containers, capillaries, pads, slices, films, plates, slides, etc. The substrate may have any convenient shape, such as a disc, square, sphere, circle, etc. [Emphasis added.]

See also page 14, line 13 which is material incorporated by reference from U.S. Patent 5,143,854, and added to the instant specification at this page and line in the Amendment dated August 22, 2003:

> A substrate is a material having a rigid or semi-rigid surface. In many embodiments, at least one surface of the substrate will be substantially flat, although in some embodiments it may be desirable to physically separate synthesis regions for different polymers with, for example, wells, raised regions, etched trenches, or the like. According to other embodiments, small beads may be provided on the surface which may be released upon completion of the synthesis. [Emphasis added.]

The Examiner is also respectfully directed to page 74, lines 3-9:

> In particular, at least four different substrate preparation procedures are available for treating a substrate surface. They are the standard VLSIPS™ Technology method, polymeric substrates, Durpaore™, and synthetic beads or resins. [Emphasis added.]

Concerning the Examiner's statements questioning support in the specification for bead, sphere or particle density or numbers, the language quoted above shows that the specification contemplates that substrates have regions of oligonucleotide synthesis or attachment and that the number of these regions can be of very high, for instance in excess of about 10^2, 10^3, 10^4, 10^5, 10^6 or more regions. Further, these sections of the specification disclose that beads, particles or spheres are types of substrates and that each bead, particle or sphere may be a region for oligonucleotide synthesis or attachment. It is evident that each bead will contain a unique nucleic acid species (oligonucleotide) and therefore consist of a synthesis region as one nucleic acid species would be synthesized per bead. The purpose of the inventions disclosed in the present specification is that one sequence should be present in each synthesis region, in this case a bead, particle or sphere, so that specific binding of nucleic acids may be detected.

In sum, it is disclosed in the specification that VLSIPS and other technologies can be used to attach nucleic acids to substrates at specific regions, that VLSIPS and these technologies can make 10^2, 10^3, 10^4, 10^5, and 10^6 unique nucleic acid sequences and that these sequences can be made on a suitable number of beads wherein each bead is a

region. Applicants respectfully request that the Examiner reconsider and withdraw the present rejection on the above basis.

3. *Spheres, beads or particles with populations of different species of nucleic acids attached thereto*

The Examiner states "the specification fails to provide support for spheres, beads or particles with populations of different species of nucleic acids attached thereto." Applicants respectfully disagree. As the Examiner points out, the specification states that each probe may be attached to a single bead. If nothing else, it shows that each bead, particle or sphere is designed to have one species of unique nucleic acid attached to its surface. Applicants respectfully request that the Examiner reconsider and withdraw the present rejection on the above basis.

Applicants are interested in moving the prosecution of this application forward and for sake of expediency, cancel claim 27. Applicants do not necessarily agree with the propriety of the rejection, as the current claims should cover the same subject matter.

5. *Methods of screening large numbers of nucleic acid molecules using beads on a support*

As set forth above, the Examiner states "the skilled artisan would not have realized that applicant was in possession of a method for screening large numbers of biological polymers using beads on a support." The Examiner appears to agree that there is written description for using beads to hybridize to a target, and that beads can be attached to a substrate and have nucleic acid sequences attached thereto. The Examiner further suggests that there is no written description for hybridization when the beads are on a support. Applicants respectfully disagree. Applicants agree that there is written description for use of beads to hybridize to targets and state that it is a natural extension to the use of beads, irrespective of where they are. Applicants suggest that it is contemplated that the beads will remain on the support as stated in the above language in

the specification (see page 14, line 13+ "small beads may be provided on the surface which may be released upon completion of the synthesis." [Emphasis added.])

The Examiner also suggests that the specification does not teach how to detect sample binding to the nucleic acids when the beads are attached to a surface because the only disclosed detection method is by cell sorting. Applicants respectfully disagree. For example, the specification states that:

> ...the target may be bound to the whole collection of beads and those beads that have appropriate specific reagents on them will bind to the target. Then a sorting system may be utilized to sort those beads that actually bind the target from those that do not. This may be accomplished by presently available cell sorting devices or a similar apparatus (page 37, lines 6-12). [Emphasis added.]

In this paragraph, the use of cell sorting systems is permissive and it is clear that another "similar apparatus" could be used. In the configuration with the beads bound to a surface, other technologies are useful to detect sample (nucleic acid) binding or hybridization, such as the confocal microscope that is discussed in detail in the application. This sort of device is discussed in the specification in many different locations, *e.g.*, page 42, lines 1-7 and page 87 under "Scanning Sytem." It is also disclosed in the '854 patent which is incorporated by reference in its entirety.

Applicants also direct the Examiner to page 114, line 36 to page 115, line 29, for an example in which a flourescently-labeled bead is detected using confocal fluorescent microscopy.

5. Demonstration of Signal Capability

> Signal detection capability was demonstrated using a low-level standard fluorescent bead kit manufactured by Flow Cytometry Standards and having model no. 824. This kit includes 5.8 μm diameter beads, each impregnated with a known number of fluorescein molecules.
>
> One of the beads was placed in the illumination field on the scan stage in a field of a laser spot which was initially shuttered. After being positioned in the illumination field, the photon detection equipment was turned on. The laser beam was unblocked and it interacted with the particle bead, which then fluoresced. Fluorescence curves of beads impregnated with 7,000 and

29,000 fluorescein molecules, are shown in FIGS. 11A and 11B, respectively of Pirrung et al. (1992) U.S. Pat. No. 5,143,854. On each curve, traces for beads without fluorescein molecules are also shown. These experiments were performed with 488 nm excitation, with 100 .mu.W of laser power. The light was focused through a 40 power 0.75 NA objective.

The fluorescence intensity in all cases started off at a high value and then decreased exponentially. The fall-off in intensity is due to photobleaching of the fluorescein molecules. The traces of beads without fluorescein molecules are used for background subtraction. The difference in the initial exponential decay between labeled and nonlabeled beads is integrated to give the total number of photon counts, and this number is related to the number of molecules per bead. Therefore, it is possible to deduce the number of photons per fluorescein molecule that can be detected. This calculation indicates the radiation of about 40 to 50 photons per fluorescein molecule are detected.

In sum, it is evident that the specification discloses that beads can be attached to substrates and that they can have nucleic acid sequences attached thereto. It is also evident that beads may be used to hybridize to targets for detection of those targets. As shown above, the specification teaches that the beads on the support, after hybridization with labeled sample nucleic acids, can be detected with the same systems employed to detect hybridization on flat arrays. One system, confocal microscopy, is detailed in the present application and the '854 patent and is used in an example to detect fluorescent molecules on beads while the beads rest on a solid support. Consequently, Applicants assert that there is written description for present method claims and respectfully request that the Examiner reconsider and withdraw the present rejection.

Rejections under 35 U.S.C. §112, second paragraph

The Examiner has rejected the pending claims and stated that:

it is unclear whether each of the beads, spheres, particles differ in physical attributes like size, shape or color or whether the claim is intended to merely mean 1000 spheres, beads or particles. Further, it is unclear how the recitation "having different species of nucleic acids directly or

indirectly attached thereto" because it is unclear whether there are 1000 different nucleic acids on the 1000 spheres, beads or particles or whether there may be a population of 2 nucleic acids on a 1000 spheres such that the same nucleic acid exists on 500 of the spheres, beads or nucleic acids and a different species is on the other 500 particles, spheres or beads (page 6 of the Office Action).

Applicants respectfully submit that they have cleared up any confusion with the word "different" by deleting that word. Furthermore, they have attempted to clarify what is on the bead by amending the claim to recite "unique" as it applies to the nucleic acid that is attached to the bead. Applicants respectfully request that the Examiner reconsider and withdraw the rejection on this basis.

Rejection based on 35 U.S.C. §102(b)

The Examiner has rejected claims 26-27, 30-35, 39-42, 45-47 based on 35 U.S.C. §102(b) over Matteucci *et al.* The Examiner generally outlines the reference, but then acknowledges that it does not show "1000 unique nucleic acid species upon 1000 beads." Applicants' current claims are structured so that they recite such a limitation. Consequently, Applicants request that the Examiner reconsider and withdraw the present rejection based on Matteucci *et al.*

CONCLUSION

Applicants respectfully request reconsideration and withdraw of the rejections. Applicants have shown that there is written description for the number of beads, the density and the use of the beads on a support for hybridization assays. Additionally, Applicants have clarified the claim language to eliminate any confusion and to avoid Matteucci *et al.* Consequently, Applicants request that the Examiner pass this case to issuance.

Applicants respectfully submit that the delay in issuing this application after payment of the issue fee on October 17, 2003 has substantially lessened the term available in the resulting patent. This delay was through no fault of Applicants and

Applicants respectfully request that the issue fee payment held at the Office be immediately applied upon issuance of a Notice of Allowance and Issue Fee Due.

Except for issue fees payable under 37 CFR §1.18, the commissioner is hereby authorized by this paper to charge any additional fees during the pendency of this application including fees due under 37 CFR §1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 CFR §1.136(a)(3).

If the Examiner has any further questions relating to this Reply or to the application in general, she is respectfully requested to contact the undersigned by telephone so that allowance of the present application may be expedited.

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS LLP

Dated: August 19, 2004

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EXHIBIT I

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RECEIVED MAY 21 1990 LICENSING & REVIEW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:)
Michael C. Pirrung et al.) RECEIVED GROUP 180
Serial No. 492,462) JUL 13 1990
Filed: March 7, 1990)
For: VERY LARGE SCALE IMMOBILIZED POLYMER SYNTHESIS) PETITION AND FEE AUTHORIZATION FOR LICENSE FOR FOREIGN FILING
) San Francisco, CA 94105

COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

Mrs. Miller need this license today. Thank you

PLEASE NOTE THIS PETITION REQUESTS EXPEDITED

HANDLING AND A TELEPHONE REPORT

MAY 23 1990 495463

Sir:

Petition is hereby made in duplicate for a license under 37 CFR 5.12(b) for the foreign filing of the subject matter of the above-identified U.S. patent application. A redlined copy of the pending United States application and its re-typed counterpart as it is expected to be foreign-filed are attached hereto to assist in the handling of this petition. This application is a continuation-in-part of Application Serial No. 362,901, filed June 7, 1989 for which foreign filing is permitted by virtue of the passing of 6 months from its filing date.

It is requested that the duplicate copy of the petition be returned with the license or other action on the petition.

It is believed that this invention is clearly of no interest from a security standpoint as it relates to a method and device for forming diverse chemical sequences such as amino acid sequences on a solid substrate. The substrate is then used in, for example, ligand/antiligand studies.

USSN 492,462

G 11258 05/18/90 07492462 20-1430 110 160 120.00CH

Expedited handling of this petition for license is requested and the $120.00 fee therefor is to be charged to Deposit Account No. 20-1430. A duplicate copy of this petition is attached.

Please notify petitioner of the issuance of the license by contacting [redacted] Ms. Annette Masiello at (703) 521-7060.

Respectfully submitted,

TOWNSEND and TOWNSEND

Date: 4/17/90

By: Vern Norviel
Reg. No. 32,483

Enclosures:

1. Redlined copy of USSN 362,901
2. Copy of re-typed counterpart

VN:dc
WP50/11509/A-1-1.P05

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